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EXAMINER

VENCI, DAVID J

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 09/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/682,199	HERMENTIN ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on July 25, 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16-35 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on July 25, 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Examiner acknowledges Applicants' reply, filed July 25, 2005, which amended claims 16-23 and 28-32, and added new claim 35.

Currently, claims 16-35 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

Examiner acknowledges Applicants' receipt of color drawings, submitted July 25, 2005. However, color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

The drawings are objected to because Fig. 8, submitted July 25, 2005, has poor resolution, which renders it unreadable. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

Claims 16-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 16, the recitation of "multimer bands" lacks antecedent basis.

In claim 16, the recitation of "multimer bands are visualized by immunostaining after a Western blot analysis" is indefinite because it is not clear how "multimer bands" within said agarose gel are visualized after blotting. The purpose of immunostaining a blotted gel is not clear.

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In claim 16, the recitation of "multimer bands are visualized... using a specific antibody-enzyme conjugate on a blotting membrane" is indefinite because it is not clear how "multimer bands" within said agarose gel are visualized "using a specific antibody-enzyme conjugate on a blotting membrane"

In claim 16, the recitation of "submarine" is indefinite because it is not clear what property or characteristic of gel electrophoresis is "submarine" or whether claim 1 requires a naval vessel (see e.g. specification p. 5, line 37, "catamaran") or a large hoagie-like sandwich (see e.g. specification p. 9, line 9, "blot sandwich").

In claim 16, the recitation of "by immunostaining" is indefinite because it is not clear whether "immunostaining" is a required step limitation. It is not clear whether/how "immunostaining" is incidental to "visualized".

In claim 16, the recitation of "by immunostaining after a Western blot analysis" is indefinite because it is not clear whether the step of "immunostaining" is completed during and/or prior to the step of fractionation by submarine electrophoresis. It is not clear whether "immunostaining" is performed during and/or after "Western blot analysis". It is not clear why it is necessary to repeat "immunostaining" after Western blot analysis.

In claim 16, the recitation of "using a specific antibody-enzyme conjugate" is indefinite because the step(s) required in the process of "using" is/are not clear. It is not clear whether said antibody-enzyme conjugate is used during both immunostaining and Western blot analysis.

In claim 16, the recitation of "optionally" is indefinite because it is not clear whether verbiage subsequent to "optionally" contains required claim limitations.

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In claim 29, the recitation of "the agarose gel employed for the Western blot analysis" lacks antecedent basis. In addition, the recitation of "chosen from" is indefinite because it is not clear whether a Markush-type claim is intended. In addition, the recitation of "the blotting process" lacks antecedent basis.

In claims 31-32 and 35, the recitations of "after blue staining", "after immunostaining", and "prior to the staining" result in comparative type mismatch in claim 16.

In claim 35, the recitation of "the staining" lacks antecedent basis.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16, 19-26, 30, 32 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Krizek & Rick, 97 THROMB. RES. 457 (2000).

Krizek & Rick teach a determination of von Willebrand factor (see Title) using a continuous agarose gel (see p. 458, col. 1, *1.2 Preparation of SDS-Agarose Gels*) and a blotting membrane immunostained with an antibody-enzyme conjugate dye (see p. 459, col. 1, *1.7 Immunolocalization of vWF Multimers*).

With respect to claims 20-25, it would have been obvious to a person of ordinary skill in the art to modify temperature ranges and agarose concentrations in order to perfect electrophoretic separation, since it

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has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. See *In re Aller*, 105 USPQ 233 (CCPA 1955).

Claim Rejections - 35 USC § 103

Claims 16-27 and 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Connaghan et al., 65 BLOOD 589 (1985), in view of Krizek & Rick, 97 THROMB. RES. 457 (2000).

Connaghan et al. teach a determination of von Willebrand factor and fibrinogen (see Fig. 1) (see e.g. Fig. 2, "densitometric analysis") using a continuous agarose gel (see p. 590, col. 2, *Gel Electrophoresis*) stained with a dye (see p. 591, col. 1, "Coomassie Blue R-250").

Connaghan et al. do not perform Western analysis using a specific antibody-enzyme conjugate. However, Krizek & Rick teach a method for detecting von Willebrand factor by Western blot (see Abstract) using an antibody-horseradish peroxidase conjugate (see p. 459, col. 1, 1.7. *Immunolocalization of vWF Multimers*). Therefore, it would have been obvious for a person of ordinary skill in the art to modify the determination of von Willebrand factor and fibrinogen of Connaghan et al. with the use of Western analysis because Krizek & Rick discovered several advantages to their method, including rapid processing, simplicity of gel preparation, high sensitivity to low concentrations of von Willebrand Factor, and elimination of radioactivity (see Abstract).

With respect to claims 20-25, Connaghan et al. teach a method wherein the agarose gel has 2% by weight agarose and the electrophoresis is carried out at 10 degrees Celsius (see p. 590, col. 2, *Gel Electrophoresis*).

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With respect to claim 32, Krizek & Rick teach a method wherein the blot bands are quantified (see p. 459, col. 2, 1.9. *Densitometric Analysis*).

With respect to claim 33, Connaghan et al. teach a method wherein the gel is laminated (see p. 591, col. 1, "gel was then dried on a slab gel drier", *noting* that "slab gel drier" necessarily teaches a multi-layered gel laminate, e.g. including Whatmann filter paper, and would be so recognized by persons of ordinary skill in the art.)

With respect to claim 34, Krizek & Rick teach a method wherein the blot is laminated (see p. 459, col. 1, *Visualization of VWF Multimers*, "wrapped in plastic wrap").

Claims 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Connaghan et al., 65 BLOOD 589 (1985), and Krizek & Rick, 97 THROMB. RES. 457 (2000) as applied to claims 16-17, and further in view of Riley & Provonchee (US 6,090,255).

Connaghan et al. and Krizek & Rick teach a determination of von Willebrand factor and fibrinogen as substantially described supra. The aforementioned references do not teach an agarose gel having a "backing sheet."

However, Riley & Provonchee teach a package (see Title) of agarose gels (see col. 2, lines 35-38) having support sheets (see e.g. Fig. 3, "support sheet 24", "spacers 26") for providing support to fragile agarose gels. Therefore, it would have been obvious for a person of ordinary skill in the art to modify the method of Connaghan et al. and Krizek & Rick with the use of backing sheets because Riley & Provonchee discovered that backing sheets provides a rigid support for gels, which minimizes inadvertent bending

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and damage to gels during shipment and facilitates the removal of gels from the packaging (see col. 2, lines 7-43).

Claims 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krizek & Rick, 97 THROMB. RES. 457 (2000) in view of Riley & Provonchee (US 6,090,255).

Krizek & Rick teach a determination of von Willebrand factor as substantially described supra. Krizek & Rick do not teach an agarose gel having a "backing sheet."

However, Riley & Provonchee teach a package (see Title) of agarose gels (see col. 2, lines 35-38) having support sheets (see e.g. Fig. 3, "support sheet 24", "spacers 26") for providing support to fragile agarose gels. Therefore, it would have been obvious for a person of ordinary skill in the art to modify the method of Krizek & Rick with the use of backing sheets because Riley & Provonchee discovered that backing sheets provides a rigid support for gels, which minimizes inadvertent bending and damage to gels during shipment and facilitates the removal of gels from the packaging (see col. 2, lines 7-43).

Response to Arguments

In prior Office Action, claim 16 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite because "the multimer bands" lacked antecedent basis. In response, Applicants argue, "it is understood that the multimers will form various bands on the gel, or multimer bands" (see Applicants' reply, p. 8, lines 5-6) (internal quotations omitted). Applicants' argument has been carefully considered but is not persuasive.

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The plain language of claim 16 neither explicitly recites, nor is it inherent, that vWF or fibrinogen will form multimer bands in a gel. One cannot reasonably argue that all gels inherently have multimer bands, or that all electrophoretic fractionations inherently result in multimer bands, or that all electrophoretic fractionations of vWF or fibrinogen inherently result in multimer bands. Thus, "multimer bands" are not necessarily or inherently present in all gels, all electrophoretic fractions, or even all electrophoretic fractionations of vWF or fibrinogen.

From the plain language of claim 16, there is no apparent causal relationship between (1) vWF or fibrinogen being (2) electrophoretically separated, resulting in (3) multimer bands, such that persons of ordinary skill would come to the dichotomous conclusions that the recited "multimer bands" may be, or may not be, derived from vWF but not fibrinogen, or both vWF and fibrinogen, or neither vWF nor fibrinogen. Such a dichotomy results in a claim whose scope is wholly indefinite.

Thus, the recitation of "multimer bands" without antecedent basis is indefinite.

In prior Office Action, claim 16 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "submarine." In response, Applicants argue that the term "submarine" modifies the term "electrophoresis". However, Applicants do not define the term "submarine".

In addition, Applicants argue that Chen (US 5,549,806) provides clarity for Applicants' usage of the term "submarine" such that persons of ordinary skill would understand the meaning of the term "submarine" on its open face. However, Applicants point to nothing in Chen that provides clarity for Applicants' usage of the term "submarine" in the instant application.

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Finally, Applicants slice the scope of the term "submarine" to something that isn't a "blot sandwich" (see Applicants' reply, p. 9, first full paragraph). However, Applicants do not affirmatively define what is a "submarine" by positively describing those characteristics that characterize a "submarine".

According to MPEP 2173.05(a), when there is more than one definition for a term, it is incumbent upon applicant to make clear which definition is being relied upon to claim the invention. Examiner posits that Applicants' argumentation set forth on p. 9, first full paragraph, is not sufficient to satisfy Applicants' burden for the reasons set forth. Until the meaning of a term or phrase used in a claim is clear, a rejection under 35 U.S.C. 112, second paragraph is appropriate. *Id.*

In prior Office Action, claim 29 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the recitation of "the agarose gel employed for immunostaining" and "the blotting process" lacked antecedent basis. Applicants' amendment and argumentation are not sufficient to overcome this rejection. Examiner posits that an "agarose gel" is not inherent to "Western blot analysis", insofar as "Western blot analysis" may simply involve flicking the on/off switch of a densitometer and looking at a computer screen, or finger testing the temperature of the transfer buffer by flicking the switch of the power source.

In prior Office Action, claims 16-27 and 30-34 were rejected under 35 U.S.C. 103(a) as being unpatentable over Connaghan et al., 65 BLOOD 589 (1985), in view of Krizek & Rick, 97 THROMB. RES. 457 (2000). In response, Applicants attempt to distinguish their invention from the prior art by observing that the prior art teaches "standard horizontal gels" whereas Applicants' invention is a "submarine electrophoresis procedure" (see Applicants' reply, paragraph bridging pp. 13-14; p. 15, lines 7-10).

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Notwithstanding issues of indefiniteness of the term "submarine", addressed supra, the prior art clearly teaches an electrophoresis procedure. Applicants' reliance on the example of a "submarine electrophoresis procedure" described in Applicants' specification on p. 7, lines 6-26, is not instructional because Examiner is unable to discern a naval vessel (see e.g. specification p. 5, line 37, "catamaran") or a large hoagie-like sandwich (see e.g. specification p. 9, line 9, "blot sandwich") in said example.

In addition, Applicants' posit that prior art teaches or acquiesces to using gels with lumps, whereas Applicants' invention delivers the art from lumps (see Applicants' reply, p. 14, lines 1-5; p. 15, lines 10-12). Examiner respectfully disagrees with Applicants' subjective interpretation of two-dimensional black and white pictures, probably photocopied many times over, depicting gels and blots with lumps. Absent objective evidence to the contrary, Examiner subjectively interprets said two-dimensional black and white pictures (photocopies) depicting gels and blots without lumps.

Examiner acknowledges Applicants' observation that Connaghan et al. do not describe multimer bands of fibrinogen (see Applicants' reply, p. 14, first full paragraph, p. 15, penultimate paragraph). However, Examiner is somewhat confused by Applicants' conclusion that, since Connaghan et al. do not describe fibrinogen multimers, persons of ordinary skill would concluded that dyes cannot be used to determine multimers effectively. In fact, Connaghan et al. does use dyes to effectively determine multimer bands of vWF, BSA, and fibrin (see Figs. 1 and 2).

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Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv



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09/18/05